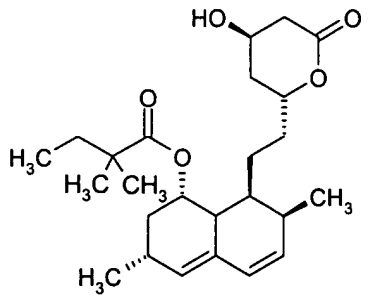
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

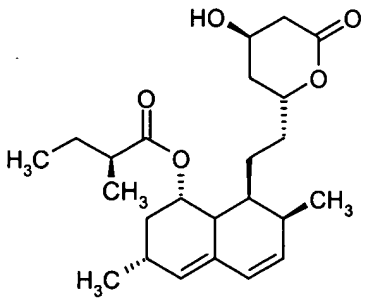


----- I

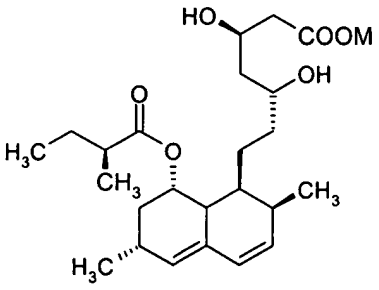
1. (original) A process for the preparation of simvastatin of formula I:

which comprises the steps of:

a) reacting compound of formula II (lovastatin) or formula III:



----- II



----- III

wherein M is H, metal ion or NH_4,

with the compound of formula IV:

HNR_1R_2 ---------- IV

wherein

R_1 is $-R_5-X-R_6$ wherein

R_5 is alkyl, arylalkyl or cycloalkyl,

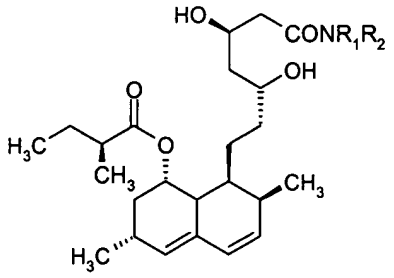
X is O or S and

R_6 is alkyl, arylalkyl, cycloalkyl or aryl; and

R_2 is independently selected from H, alkyl, cycloalkyl, arylalkyl and a group as defined for R_1;

or R1 and R2 may be bonded to form a cyclic ether or cyclic thio ether;

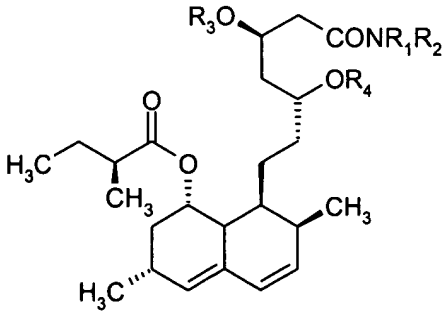
to produce a compound of formula V:



------ V

wherein R_1 and R2 are as defined above,

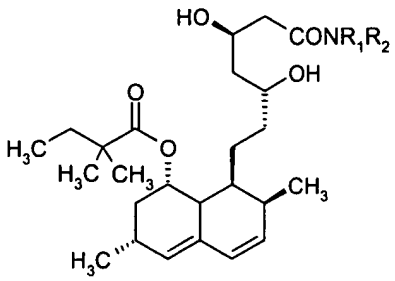
(b) optionally protecting the two hydroxyl groups of the compound of the formula V to produce a compound of the formula VI:



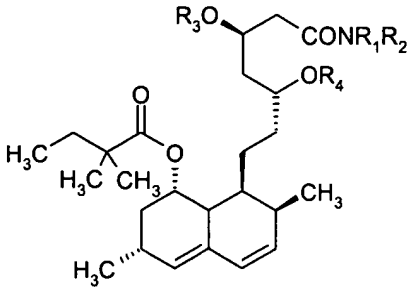
------ VI

wherein R3 and R4 represents suitable protecting groups,

(c) methylating said compound of formula V or VI to give a compound of formula VIIa or VIIb:



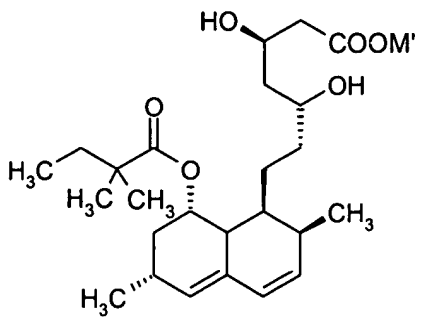
----- VIIa



----- VIIb

wherein R_1, R_2, R_3 and R_4 are as defined above,

(d) hydrolyzing the amide group if the product of the above step is said compound of formula VIIa or deprotecting the two protected hydroxy groups prior to hydrolysis if the product of the above step is said compound of formula VIIb, optionally treating the hydrolyzed product with aqueous ammonia, to produce a compound of formula VIII:



----- VIII

wherein M' is a metal such as sodium or potassium or NH_4, and

(e) lactonizing said compound of the formula VIII to produce simvastatin of formula I.

2. (original) A process according to claim 1, wherein the hydroxy groups are not protected before methylation.

3. (currently amended) A process according to claim 1 ~~and~~ 2, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is selected from H, methoxyethyl, ethoxyethyl and methoxymethyl.

Cancel Claims 4 through 28.

29. (new) A process according to claim 2, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is selected from H, methoxyethyl, ethoxyethyl and methoxymethyl.

30. (new) A process according to claim 3, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is H.

31. (new) A process according to claim 29, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is H.

32. (new) A process according to claim 1, wherein R_1 is methoxyethyl and R_2 is H.

33. (new) A process according to claim 2, wherein R_1 is methoxyethyl and R_2 is H.

34. (new) A process according to claim 3, wherein R_1 is methoxyethyl and R_2 is H.

35. (new) A process according to claim 29, wherein R_1 is methoxyethyl and R_2 is H.

36. (new) A process according to claim 30, wherein R_1 is methoxyethyl and R_2 is H.

37. (new) A process according to claim 31, wherein R_1 is methoxyethyl and R_2 is H.

38. (new) A process according to claim 1, wherein methylation is carried out using an alkali metal amide and a methyl halide.

39. (new) A process according to claim 38, wherein the alkali metal is lithium, sodium or potassium; and the methyl halide is methyl iodide, methyl chloride or methyl bromide.

40. (new) A process according to claim 38, wherein the alkali metal amide is lithium pyrrolidide and the methylhalide is methyl iodide.

41. (new) A process according to claim 39, wherein the alkali metal amide is lithium pyrrolidide and the methylhalide is methyl iodide.

42. (new) A process according to claim 1, wherein the starting compound is lovastatin of the formula II.

43. (new) A process according to claim 1, wherein R_3 and R_4 represent silyl protecting groups.

44. (new) A process according to claim 43, wherein the silyl protecting groups are selected from t-butyldimethylsilyl and trimethylsilyl groups.

45. (new) A process according to claim 1, wherein:

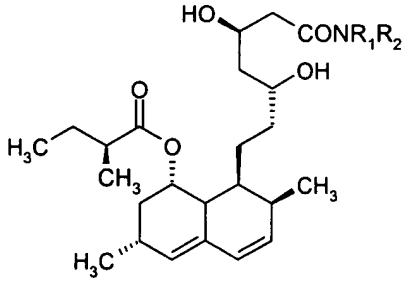
i) lovastatin is treated with methoxyethyl amine in an organic solvent to produce the compound of the formula V wherein R_1 is methoxyethyl- and R_2 is H,

ii) methylating the product obtained in the previous step with lithium pyrrolidide in tetrahydrofuran and methyl iodide to produce the compound of the formula VIIa wherein R_1 is methoxyethyl- and R_2 is H,

iii) hydrolyzing the product obtained in the previous step with a strong base to obtain the compound of the formula VIII,

iv) adding aqueous ammonia to the product obtained in the previous step to produce simvastatin ammonium salt, and

v) lactonizing the product obtained in the previous step to produce simvastatin.



------ V

46. (new) A compound of the formula V:

wherein

R_1 is $-R_5-X-R_6$ wherein

R_5 is alkyl, arylalkyl or cycloalkyl,

X is O or S and

R_6 is alkyl, arylalkyl, cycloalkyl or aryl; and

R_2 is independently selected from H, alkyl, cycloalkyl, arylalkyl and a group as defined for R_1;

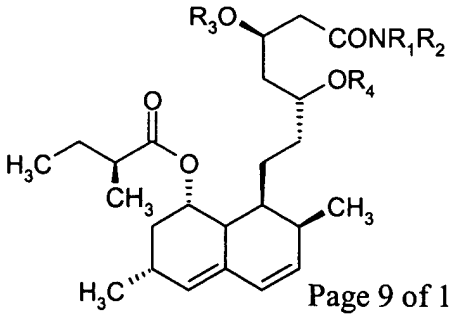
Or R_1 and R_2 may be bonded to form a cyclic ether or cyclic thio ether.

47. (new) The compound of the claim 46, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is selected from H, methoxyethyl, ethoxyethyl and methoxymethyl.

48. (new) The compound of claim 47, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is H.

49. (new) The compound of claim 48, wherein R_1 is methoxyethyl and R_2 is H.

50. (new) A compound of the formula VI:



------ VI

wherein R_1 and R_2 are as defined in formula V of claim 46;
and R_3 and R_4 represent suitable protecting groups.

51. (new) The compound of claim 50, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, R_2 is selected from H, methoxyethyl, ethoxyethyl and methoxymethyl and R_3 and R_4 are selected from silyl protecting groups such as t-butyldimethylsilyl and trimethylsilyl groups.

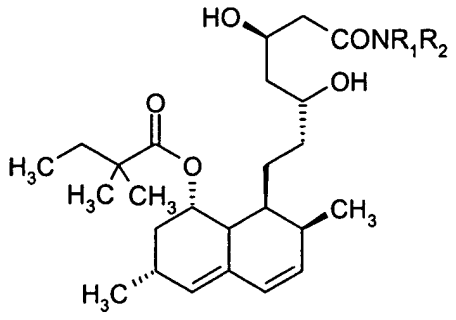
52. (new) The compound of claim 50, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is H.

53. (new) The compound of claim 51, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is H.

54. (new) The compound of claim 52, wherein R_1 is methoxyethyl and R_2 is H.

55. (new) The compound of claim 53, wherein R_1 is methoxyethyl and R_2 is H.

56. (new) The compound of the formula VIIa:



----- VIIa

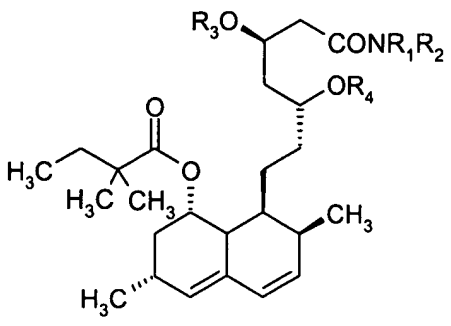
wherein R_1 and R_2 are as defined in the formula V of claim 46.

57. (new) The compound of the claim 56, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is selected from H, methoxyethyl, ethoxyethyl and methoxymethyl.

58. (new) The compound of claim 57, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is H.

59. (new) The compound of claim 58, wherein R_1 is methoxyethyl and R_2 is H.

60. (new) A compound of the formula VIIb:



----- VIIb

wherein R1, R2, R3 and R4 are as defined in formula VI of claim 50.

61. (new) The compound of claim 60, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, R_2 is selected from H, methoxyethyl, ethoxyethyl and methoxymethyl and R_3 and R_4 are selected from silyl protecting groups such as t-butyldimethylsilyl and trimethylsilyl groups.

62. (new) The compound of claim 60, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is H.

63. (new) The compound of claim 61, wherein R_1 is selected from methoxyethyl, ethoxyethyl and methoxymethyl, and R_2 is H.

64. (new) The compound of claim 62, wherein R_1 is methoxyethyl and R_2 is H.

65. (new) The compound of claim 63, wherein R_1 is methoxyethyl and R_2 is H.